Third Generation PSA



IMMULITE* Third Generation PSA

English

when used in conjunction with digital rectal examination (DRE) in men aged 50 years quantitative measurement prostatewith the IMMULITE Analyzer - for the or older. This assay is further indicated as an aid in the detection of prostate cancer specific antigen (PSA) in human serum, as management of prostate cancer patients an adjunctive test to aid in the Intended Use: For in vitro diagnostic use

Catalog Number: LKUP1 (100 tests), LKUPS (500 tests)

Test Code: sPS Color: Red

restricts this device to sale by or on the Caution: In the United States, Federal law order of a physician.

specimen determined with different specificity. The results reported by the assays can vary due to differences in The concentration of PSA in a given interchangeably. Before changing Values obtained with different PSA include the identity of the assay used assay methods and reagent serially monitored. the baseline values for patients being assays, the laboratory must confirm assays cannot be used aboratory to the physician must

Summary and Explanation

sequence of PSA was reported, and the gene has been cloned. PSA is it contains approximately 10% carbohydrate by weight. 2 The amino acid in 1979, is a glycoprotein monomer with protease activity. 12 PSA has an isoelectric Prostate specific antigen (PSA), first identified and characterized by Wang, et al from PAP and does not exhibit enzymatic weight of approximately 33-34 kilodaltons point of approximately 6.9 and a molecular phosphatase activity biochemically and immunologically distinct

prostatic ductal epithelium and in PSA is localized in the cytoplasm of secretions of the ductal lumina. Because

> prostatic hypertrophy, and inflammatory conditions of other adjacent genitourinary it can be recovered and purified both from PSA is a secretory protein of the prostate, PSA has been found to be exclusively prostatic tissue and from seminal plasma patients with prostate cancer, benign elevated serum PSA has been found in associated with prostate tissue;17 and nonprostatic carcinoma, healthy women or women with cancer. 5.8 tissues, but not in healthy men, men with

observed in patients with benign prostatic hypertrophy (BPH), nor is it staging. The combination of PSA elevated PSA concentrations are also screen for prostate cancer because Serum PSA alone is not suitable as a findings may provide a better method of ultrasonography in the event of abnormal measurement and rectal examination with recommended as a guide in disease detecting prostate cancer: the result is offers several advantages over digital examination alone. Measurement of PSA detecting prostate cancer than rectal patients than other procedures.* the procedure is more acceptable to independent of the examiner's skill, and objective, quantitative, and obtained rectal examination or ultrasonography in

surgical or medical treatment of prostate cancer. 16,11 Persistent elevation of PSA or persistent disease in patients following PSA can be useful in detecting metastatic indicative of recurrent or residual disease. 12-16 Hence, PSA is widely pretreatment PSA concentrations is following treatment or an increase in the Determinations of total immunoreactive accepted as an aid in the management of prostate cancer patients. 12-16

expectancy, as well as younger men who offered annually, beginning at age 50, to are at high risk. Patients should be given men who have at least a 10-year life test and digital rectal examination be The American Cancer Society has Men in high risks groups, such as those benefits of early detection and treatment information regarding potential risks and recommended that both the PSA blood with two or more affected first-degree

relatives may consider screening at a younger age, perhaps 45.27

Principle of the Procedure

Incubation Cycles: 2 × 30 minutes. Sequential Immunometric Assay.

Specimen Collection

PSA level using conventional PSA assays. 15.20 Therefore, when possible, examination. obtain PSA samples before digital rectal of an effect of digital rectal examination on shown conflicting results on the existence levels persisting for up to 3 weeks using conventional PSA assays. 18 Studies have prostate gland may lead to elevated PSA massage, since manipulation of the biopsy, prostatectomy or prostatic Samples should be obtained before

complete clot forms may result in the presence of fibrin. To prevent erroneous increased clotting time. anticoagulant therapy, may require those from patients receiving samples. Some samples, particularly taken place prior to centrifugation of ensure that complete clot formation has results due to the presence of fibrin, Centrifuging serum samples before a

cup must contain at least 100 µL more Volume Required: 50 µL serum. (Sample than the total volume required.)

Store at -18°C or colder if samples are to be assayed after extended storage. Storage: 24 hours at 2-8°C.21

Warnings and Precautions

For in vitro diagnostic use.

accordance with applicable laws. Reagents: Store at 2-8°C. Dispose of in

B surface antigen; and for antibodies to for antibodies to HIV 1 and 2; for hepatitis materials derived from human blood were transmitting infectious agents. Source tested and found nonreactive for syphilis; all components as if capable of Follow universal precautions, and handle

preservative. On disposal, flush with large 0.1 g/dL, has been added as a volumes of water to prevent the buildup of Sodium azide, at concentrations less than

> and copper plumbing. potentially explosive metal azides in lead

contamination and exposure to direct Chemiluminescent Substrate: Avoid sunlight. (See insert.)

Water: Use distilled or delonized water.

Materials Supplied

barcode labels are needed for the assay. Components are a matched set. The

Third Generation PSA Test Units

PSA antibody. Stable at 2-8°C until bead coated with monoclonal murine anti-Each barcode-labeled unit contains one expiration date.

LKUP1: 100 units. LKUP5: 500 units.

cutting along the top edge, leaving the protect from moisture. ziplock ridge intact. Reseal the bags to temperature before opening. Open by Allow the Test Unit bags to come to room

(LUPA LUPB) Third Generation PSA Reagent Wedges

LKUP1: 1 set. LKUP5: 5 sets. within 30 days after opening when stored expiration date. Recommended usage is and refrigerated; stable at 2-8°C until buffer, with preservative. Store capped (bovine call intestine) conjugated to polyclonal goat anti-PSA antibody in buffer/serum matrix, with preservative. LUPB: 6.5 mL alkaline phosphatase as indicated. With barcodes. LUPA: 6.5 mL protein

Third Generation PSA Adjustors (LUPL,

or for longer storage (aliquotted) at -20°C Stable at 2-8°C for 30 days after opening, PSA in a serum matrix, with preservative. Two vials (Low and High), 3 mL each, of LKUP1: 1 set. LKUP5: 2 sets.

Supplied Separately Kit Components

30 days after opening, or for longer (aliquotted) at -20°C. matrix, with preservative, for the dilution of patient samples. Stable at 2-8°C for 25 mL PSA-free nonhuman serum/buffer PSA Semple Diluent (LPSZ)

LKPM: Probe Cleaning Kit LPWS2: Probe Wash Module LSCP: Sample Cups (disposable) LCHx-y: Sample Cup Holders (barcoded) LSUBX: Chemiluminescent Substrate LSCC: Sample Cup Caps (optional)

PSA Control Module LUPCM: Single-level Third Generation TMCO: Tri-level, multi-constituent control

Also Required

Sample transfer pipets, distilled or deionized water, controls.

Assay Procedure

preparation, setup, dilutions, adjustment See the IMMULITE Operator's Manual for assay and quality control procedures.

Adjustment Interval: 4 weeks.

Quality Control Samples: Use controls or sample pools with at least two levels (low and high) of PSA.

The study demonstrated that PSA testing,

of Prostate Cancer **Expected Values in Detection**

1477 men, aged 50 or older. Of these, 64 sites for prostate cancer detection (<1%) were other and 14 (<1%) provided (4%) were Asian; 242 (16%) were African purposes, samples were collected from In two retrospective studies at two clinica biopsied for elevated (> 4.0 ng/mL) PSA examination (DRE). Of these, 88 were patients also underwent digital rectal no ethnic information. 1468 out of 1477 American; 1150 (78%) were Caucasian; 7 and/or suspicious DRE. The following table summarizes these clinical studies

2 5 5	2 0 8 2 0 8	Caron of	% Positive Biopsies (95%, Cr)
All Subjects	b		
1488	8	ઝુ	39.8%
PSA > 4.0			
16 1	2	28	43.8%
11.0%	39.8%		(31.4%-56.7%)
DRE +			
5	31	15	48.4%
7.2%	29.2%		(31.0%-86.9%)

84.2% 0.7%	1236 9 2	PSA <= 4.0 DRE -	8.6% 38.1%	126 48 18	PSA > 4.0 DRE -	4.8% 21.1%	71 15 5	PSA <= 4.0 DRE +	2.4% 45.7%	35 16 10	SA > 4.0 DRE +	(%) (%) Cancers	
(2.8%-60.6%)	. 22.2%		(24.0%-52.6%)	37.5%		(14.2%-61.6%)	33.3%		(35.4%-82.2%)	62.5%		% Positive Biopsies (95% CI)	

detected 51% (18/35) of cancers that DRE than DRE sione. PSA determinations more effective in detecting prostate cancer when used in conjunction with DRE, was even if the DRE is negative. However, the 4 ng/mL may warrant additional testing did not; PSA elevations greater than detected 14% (5/35) of cancers that PSA also require additional testing since DRE suspicious DRE and a normal PSA may converse is also true: a subject with determinations did not.

distribution of PSA values by age decade were identified as asymptomatic subjects In the same studies, 1236 participants biopsied as well as for those subjects who PSA and DRE, and therefore, were not clinical study who had both a negative for these asymptomatic subjects in the no certainty that all of these subjects were were negative for cancer biopsy. There is The following table contains the of age-specific reference ranges are safe are presently no data proving that the use represent a truly normal population. There questionable whether these subjects interpreted with caution since it is Therefore, these data should be indeed free of prostate disease. or effective.

Distribution of		PSA	PSA
SIGNET VC.	2	Median	55° XIE
VII subjects	1236	0.98	3.28
50-59 age group	612	0.81	2.73
50-69 age group	458	1.11	3.45
≥70 age group	166	1.35	3.65

patients were tested. Shown below is the distribution of IMMULITE PSA results from 2618 samples collected from 1965 In studies performed at four clinical sites this study.

Female Sublects	Sumples of 4 4-10 10-20 20-40 >40 Subjects / 0-4 4-10 10-20 20-40 >40 Samples ng/mL ng/mL ng/mL ng/mL ng/m
	70 40
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473/473	Healthy Male Subjects	76/76	Malignant Diseases	28/28	Nonmalignant Diseases	149/149	Healthy	253/253	remain subjects
99.4% 0.6%	ıle Subj	100%	Disease	100%	ant Dise	100×		100%) OCIS
0.6%	2	ş	.	3	1505	3		9%	
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3		Ş		3		3		Ş	

333/333	8 P H	548/548	Non-Mailgr	473/473
333/333 67.9% 25.8% 5.4% 0.9% 0%		548/548 76.2% 19.3% 3.5% 0.9% 0%	Non-Malignant Diseases	473/473 99.4% 0.6% 0%
5.4%		3.5%		ş
9		0.9%		3%
3		9		Ş

Other Nor	88/88	
Other Nonprostatic Diseases	80.3% 18.2% 1.5%	Curer Prostatic Diseases
ioases	.2% 1.5%	3
	3	
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Non-Prostatic Malignancias	149/149	
	93.2% 5.4%	
	5.4%	
3	ş	
	1.3%	
	3	

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ਲ ਵਾ ਵਾ	93.0%	
3	6.1%	
Prostate Cancer (single specimens)	93.0% 6.1% 0.6% 0.3%	•
3	0.3%	
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105/758	
54.8% 11.7% 10.7% 7.5% 15.3%	(Delouis American (Section)
15.3%	

54.0%	31/200 54.0% 14%			
	Stage B	3.65	1.35	8
64.9% 9.8%	17/174	3.45	1.13	8
	Stage A	2.73	0.81	2
חקית חקיתו	Samples	3.28	0.98	36
1	Number of Subjects /	95 % XIII	PSA PSA Median 95" %ile	3

	nples
male Subtracts	•
	0-4 4-10 10-20 20-40 >40 ng/mL ng/mL ng/mL ng/mL ng/mL ng/mL
	70 70 70 70 70 70 70
	3 (A)
	70 0 14 0

raie Subjects		
53/253 100% 0% 04	0%	ş

legithy Male Subjects	76778	Malignant Diseases	28/28	Nonmalignant Diseases	149/149 100% 0%	ealthy	253/253
	100% 0%	Diseases	100% 0%	ant Dise	100%		100% 0%
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•	333/333 67.9% 25.8% 5.4% 0.9% 0%	8PH	548/548 76.2% 19.3% 3.5% 0.9% 0%	on-Mailgnant Diseases	473/473 99.4% 0.6% 0%
	67.9%		76.2%	ent Die	99.4%
	25.8%		19.3%	200	0.6%
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Other Nonprostatic Diseases	68/66 80.3% 18.2% 1.5%	
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Non-Prostatic Malignancies	93.2% 5.4%	
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312/312	on-Prost
	ion-Prostatic Malignancies
93.0% 6.1% 0.6% 0.3%	gnancie
0.6%	•
3%	

	274/274	
	42.3% 21.2% 13.1% 7.3% 16.	
	21.2%	
	13.1%	
,	7.3%	
	16.1%	

105/758	Prostate Ca
54.8% 11.7% 10.7% 7.5%	Cancer (serially monitored)
х :5	

	1965/2618	Total:	38/282	Stage D	19/102	Stage C	31/200	Stage B	17/174	Stage A	Samples	Subjects /	NUMBER OF
	1962		\$ 2%		56.9%		54.0% 14%		67.93 78.10		30/mL	î	
	275		48.2% 13.1% 11.7% 8.9%		56.9% 6.9%		14%		64.9% 9.8% 9.2% 3.5% 12.6%			10	
	နှင့် နှင့်		11.7		7.8%		12%		9.2%		ng/mt ng/mt	10-20 20-40 10-20 20-40	
	23		8.9%		8.8%		8.5%		3.5%			8	
	Ē		18.93 93.		8.8% 19.6%		8.5% 11.5%		12.6%		3 3	\$	
•		•	-	•		•		3	4	•	•		

Each laboratory should establish its own Consider these limits as guidelines only. reference ranges.

Limitations

Serum PSA concentrations should not be presence or absence of malignant interpreted as absolute evidence for the disease.

complete clinical evaluation of the patient Prediction of malignant prostatic disease which may also include serial serum PSA recurrence should be based on a determinations.

massage. biopsy, prostatectomy or prostatic Samples should be obtained before

PSA expression may be altered due to reflect the presence of residual or Consequently, a low PSA result following hormonal treatment may not adequately hormonal therapy for prostate cancer.

early detection of prostate cancer. mouse protein which can cause Some individuals have antibodies to This device is not intended to be used for recurrent disease.

assays. 22.24 Therefore, results should be may show erroneous results in such antibodies (HAMA). These specimens therapy may contain human anti-mouse monoclonal antibodies for diagnosis or specimens from patients who have antibodies derived from mice. In particular, interference in immunoassays that employ received preparations of mouse interpreted with caution for such patients

exposed to animals or animal serum included in the assay components causing can react with the immunoglobulins Heterophilic antibodies in human serum components can occur. For diagnostic interactions between rare sera and test interference; however, potential been formulated to minimize the risk of anomalous result. These reagents have interference potentially causing an products can demonstrate this type of 33.] Samples from patients routinely immunoassays. Clin Chem 1988:34:27-[See Boscato LM, Stuart MC. Heterophilic interference with in vitro immunoassays. purposes, the results obtained from this antibodies: a problem for all combination with the clinical examination, assay should always be used in patient medical history, and other findings

Performance Data

See Tables and Graphs for data representative of the assay's performance. Results are expressed in ng/mL. (Unless otherwise noted, all were generated on serum samples collected in tubes without gel barriers or clot-promoting additives.)

Calibration Range: Up to 20 ng/mL

Analytical Sensitivity: 0.003 ng/ml

Functional Sensitivity: 0.01 ng/mL, as demonstrated by the studies summarized in the Precision section. (Functional sensitivity is defined as the lowest concentration that can be measured with an interassay CV of 20%.)

High-dose Hook Effect: None up to 90,000 ng/mL.

Precision: Samples were assayed in duplicate over the course of 20 days, two runs per day, for a total of 40 runs and 80 replicates. Results are expressed in ng/ml.

PS/ Poor Poor	17	Ø	(J	*	ω	N			
second pared to -ACT to cessed	<u>6.1</u>	7.6	3.8	1.0	0.50	0.026	0.012	Mean	
In a second study, a six samples (prepared by adding known quantities of PSA-ACT to bovine serum albumin) were processed in duplicate over the course of	0.68	0.35	0.14	0.03	0.017	0.002	0.0016	SO	Within-Bun
six samples g known quar serum albun	1.2%	4.6%	3.7%	3.0%	3 4%	7.7%	13%	ઠ	Bun
mples n quantit albumir	0.88	0.37	0.16	0.04	0.020	0.002	0.0017	SO	Total
ies of	5.5%	4.9%	4.2%	4.0%	4.0%	7.7%	14%	ઇ	<u> </u>

In a second study, as ix samples (prepared by adding known quantities of PSA-ACT to bovine serum albumin) were processed in duplicate over the course of 20 days, two runs per day, for a total of 40 runs and 80 replicates. Statistics from this published study are reproduced, with means expressed in ng/mL.

	o,	U	•	ယ	N			
	3.066	0.290	0.144	0.029	0.0043	0.0030	Mean	
0.772	3 48	5.4%	4.9%	4.1%	14.4%	19.9%	CV	Within-Run
9.070	•	5.8%	6.1%	4.5%	14.7%	20.9%	Ş	Total

In a third study, conducted at Mount Sinai Hospital in Toronto, Canada, nine samples (from post-prostatectomy patients) were assayed with the IMMULITE Third Generation PSA in 13 runs over 10 days. The results are tabulated, with means and SDs expressed in ng/mL.

٥	œ	7	o	U	•	ω	N	_	
1.62	0.380	0.220	0.054	0.022	0.0145	0.0100	0.0062	0.0038	Mean
0.0809	0.0133	0.0108	0.0053	0.0030	0.0017	0.0019	0.0022	0.0009	SD
3.8%	3.5%	4.9%	10%	14%	12%	19%	35%	24%	CV

Precision Profile: The graph shows a within-run (intraassay) precision-dose profile for the IMMULITE Third Generation PSA, based on Master Curve data from four consecutive lots. Each point (open circle) represents the within-run CV, based on dose, for an individual sample, calculated from 10 or 20 replicates. The bowl-shaped contour line traces the approximate path of these points, as anchored by the zero calibrator. (The open diamonds at the upper left represent extrapolations, to 5 and 6 SDs, of the average imprecision at zero dose.)

For reference, the run-to-run (interassay or "total") CVs in the three precision studies tabulated above have been plott on the same graph, as solid squares.

9	Coefficient	ş	ź	ğ
9000 001 003 01 03 10 30 10 30 PSA NOME				MMULITE Third Generation PSA Meeter Curve (4 Lots) and Total Cve

Linearity: Samples were assayed unde various dilutions. Results are expressed ng/mL.

ı				N	ı								1
1 in 16	2 10 10	5 6	5 5 6	16 in 16	1 in 128	2 in 128	4 in 128	8 in 128	16 in 128	32 in 128	64 in 128	128 in 128	Dilution
0.033	0.061	0.127	0.243	0.498	^ 0.003	0.004	0.008	0.018	0.032	0.069	0.135	0.247	Observed
0.031	0.062	0.124	0.249	i	0.002	0.004	0.008	0.015	0.031	0.062	0.124	1	Expected
106% 106%	%8e	102%	%8¢	ı	ı	100%	100%	107%	103%	111%	109% X	1	%O/E

7 16 in 16 der 8 in 16 ed in 4 in 16 2 in 16				7	,		· L			<u>-</u>					<i>J</i>	ω	•	5 1:		ay			- A	§		Ō	Š	•	, 3		_
25		5 16	5 16	2 2	18 15 18	1516	25 16	5	3 5 6	16 in 18	1 in 128	2 in 128	4 in 128	8 in 128	6 in 128	128 128	4 in 128	28 in 128	1 5 16	2 in 16	5 5	5 16	5 5	1 in 16	2 5 64	4 in 16	æ 5 €4	5 5	25 25 27	¥ 50	Dilution
					ı						1								ı			0.958									I೧
07.7	ن ن ق	4.55	9.10	ı		0.345	0.680	1.36	2.72	1	0.018	0.036	0.073	0.145	0.290	0.580	1.16	1	0.115	0.230	0.460	0.920	1	0.011	0.023	0.046	0.092	0.184	0.367	1	Expected
	102	101%	107%	ı		105	Į Ž	38%	%	1	% 68	86%	92%	% %	92%	95%	39 %	,	80%	99%	108%	Õ,	,	Ī	100 X	113%	102×	105%	105%	1	#0%

Recovery: Samples spiked 1 to 19 with three PSA solutions (10.2, 46 and 91 ng/mL) were assayed.

			•				ယ				N				-	1
ဂ	œ	>	!	C	0	>	ن ا	c	ø	>	ı	ဂ	В	>	ı	Solution
							11.0									
							1	l				•				ı
Ž Ž	109%	104%	ı	8	105%	102%	ı	92%	95%	97%	ı	97%	% 0%	108%	1	%

Specificity: The antibody is highly specific for PSA.

NO: not detectable	Prolectin	PAP	Lactalbumin	HQ HQ	Ferritin	CEA	AFP	Compound
	200 ng/mL	1000 ng/mL	10000000 ng/mL	100000 mIU/mL	10000 ng/mL	100 ng/mL	10000 ng/mL	Amount Added
	N N	Ž	Š	Š	3	8	8	% Cross- reactivity

Bilirubin: No significant effect.

Hemolysis: No significant effect.

Method Comparison: All four of DPC's nonisotopic PSA assays were compared using Deming regression analysis. Samples used were within the working range of the assays. The table below

> as X. presents the results of the Deming regressions, with columns as Y, and rows

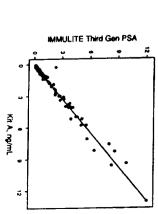
Results of Deming Regressions

#A 3rd	AMULT Genera	E 2000 ation P	O SA	3rd	IMML Gener	ILITE ation P	SA	IMM	ULITE	2000	PSA	IA	MULI	TE PS	A	
Correlation Coefficient	Intercept (95% CI)	Slope (95% CI)	5	Correlation Coefficient	Intercept (95% CI)	Slope (95% CI)	5	Correlation Coefficient	(95% CI)	Slope (95% CI)	3	Coefficient	Intercept (95% CI)	(95% CI)	3	٦
0.991	-0.06 (-0.10 to -0.02)	0.92 (0.91 to 0.94)	473	0.993	-0.06 (-0.09 to -0.02)	1.01 (1.00 to 1.03)	474	0.992	0.12 (0.08 to 0.16)	1.06 (1.05 to 1.08)	477					MMULITE PSA
0.990	-0.16 (-0.20 to -0.12)	0.86 (0.85 to 0.87)	473	0.988	-0.15 (-0.19 to -0.10)	0.94 (0.93 to 0.96)	474					0.992	-0.11 (-0.15 to -0.07)	0.94 (0.93 to 0.95)	477	IMMULITE 2000 PSA
0.990	0.00 (-0.04 to 0.04)	0.91 (0.90 to 0.92)	472					0.988	0.15 (0.11 to 0.20)	1.06 (1.05 to 1.08)	474	0.993	0.05 (0.02 to 0.09)	0.99 (0.98 to 1.00)	474	IMMULITE 3rd Generation PSA
				0.990	-0.00 (-0.05 to 0.05)	1.10 (1.09 to 1.11)	472	0.990	0.18 (0.14 to 0.23)	1.16 (1.14 to 1.17)	473	0.991	0.06 (0.02 to 0.11)	1.08 (1.07 to 1.10)	473	IMMULITE 2000 3rd Generation PSA

The assay was also compared to Kit A on 162 samples. (Concentration range: approximately 0.1 to 13 ng/mL.) By linear regression:

(IML 3rd Gen PSA) = 0.93 (Kit A) = 0.04 ng/mL r = 0.989

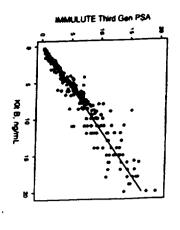
Means: 1.3 ng/mL (IML 3rd Gen PSA) 1.4 ng/mL (Kit A)



approximately 0.3 to 20 ng/mL) By linear samples. (Concentration range: The assay was compared to Kit B on 285

(IML 3" Gan PSA) = 0.85 (RQ B) + 0.16 ng/mL -0.964

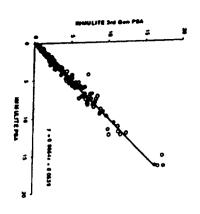
6.2 mg/mL (Kit B) 5.4 ng/mL (IMMULITE)



The assay was compared to DPC's IMMULITE PSA (LKPS) on 474 samples :uorsseuße approximately 20 ng/mL.) By linear (Concentration range: nondetectable to

(IML 3" Gan PSA) = 0.99 (IML PSA) + 0.05 ng/ml r = 0.993

2.20 ng/mL (IML 3" Gen PSA) 2.22 ng/mL (IML PSA)



References

1979;17:159-63, 2) Kuriyama M, et al. Prostatic acid phosphatase and prostate-specific antigen in prostate cancer. In: International Advances in Surgical Oncology. New York: Alan R. Lise, Inc., 1) Wang MC, et al. Purification of a human prostate specific antigen, invest Urol

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MAMULITE Third Generation PSJ

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Technical Assistance

Fax: 973.927.4101. Outside the United In the United States, contact DPC's The Quality System of Diagnostic Products Corporation is registered to ISO 9001:1994. States, contact your National Distributor Tel: 800.372.1782 or 973.927.2828 Technical Services department.

May 1, 2001 2001-04-30 (ISO 8601) Diagnostic Products Corporation 5700 West 96th Street PILKUP - 4 Los Angeles, CA 90045-5597

IMMULITE Third Generation PSA

PSA



English

management of prostate cancer patients or older. This assay is further indicated as examination (DRE) in men aged 50 years when used in conjunction with digital rectal an aid in the detection of prostate cancer specific amigen (PSA) in human serum, as the quantitative measurement of prostatean adjunctive test to aid in the with the IMMULITE 2000 Analyzer - for Intended Use: For in vitro diagnostic use

Catalog Number: L2KPS2 (200 tests), L2KPS6 (600 tests)

order of a physician. restricts this device to sale by or on the Caution: In the United States, Federal law Test Code: PSA Color: Brown

serially monitored. the besetine values for patients being Values obtained with different PSA assays, the laboratory must confirm interchangeably. Before changing assays cannot be used include the identity of the assay used. specificity. The results reported by the specimen determined with different The concentration of PSA in a given laboratory to the physician must assay methods and reagent assays can vary due to differences in

containing approximately 10% carbohydrate by weight. 12 Subsequently in 1979 is a glycoprotein monomer with protesse activity. 12 PSA has an isoelectric weight of approximately 33-34 kilodaltons point of approximately 6.9 and a molecular Prostate specific antigen (PSA) first Summary and Explanation the amino acid sequence of PSA was iffed and characterized by Wang et al

secretions of the ductal lumina. Because prostatic ductal epithelium and in PSA is localized in the cytoplasm of

enzymatic phosphatase activity distinct from PAP and does not exhibit PSA is biochemically and immunologically

reported, and the gene has been cloned.

it can be recovered and purified both from PSA is a secretory protein of the prostate, nonprostatic carcinoma, healthy women or women with cancer. 5.8 tissues but not in healthy men, men with conditions of other adjacent genitourinary prostatic hypertrophy, and inflammatory patients with prostate cancer, benign elevated serum PSA has been found in associated with prostate tissue, and PSA has been found to be primarily prostatic tissue and from seminal plasma.

independent of the examiner's skill, and offers several advantages over digital observed in patients with benign prostatic hypertrophy (BPH)*, nor is it Patients than other procedures.9 the procedure is more acceptable to objective, quantitative, and obtained detecting prostate cancer: the result is examination alone. Measurement of PSA detecting prostate cancer than rectal findings may provide a better method of measurement and rectal examination with staging. The combination of PSA Serum PSA alone is not suitable as a rectal examination or ultrasonography in utrasonography in the event of abnormal recommended as a guide in disease elevated PSA concentrations are also screen for prostate cancer because

accepted as an aid in the management of prostate cancer patients. 12-16 Concurrent measurement of PAP may contribute disease. 12-16 Hence PSA is widely Pretreatment PSA concentrations is treatment or an increase in the Persistent elevation of PSA following treatment of prostate cancer, 10.11 in patients following surgical or medical detecting metastatic or persistent disease PSA determinations can be useful in additional information. 17 indicative of recurrent or residual

offered annually, beginning at age 50, to Men in high risks groups, such as those benefits of early detection and treatment. information regarding potential risks and are at high risk. Patients should be given expectancy, as well as younger men who men who have at least a 10-year life test and digital rectal examination be recommended that both the PSA blood The American Cancer Society has

IMMULITE 2000 PS

relatives may consider screening at a younger age, perhaps 45.27 with two or more affected first-degree

Principle of the Procedure Immunometric Assay.

Incubation Cycles: 1 × 30 minutes.

Specimen Collection

massage, since manipulation of the prostate gland may lead to elevated PSA biopsy, prostatectomy or prostatic Samples should be obtained before levels persisting for up to 3 weeks. 18

the existence of an effect of digital rectal examination on PSA level. 1920 Therefore, before digital rectal examination. when possible, obtain PSA samples Studies have shown conflicting results on

complete clot forms may result in the presence of fibrin. To prevent erroneous taken place prior to centrifugation of increased clotting time. anticoagulant therapy, may require samples. Some samples, particularly ensure that complete dot formation has results due to the presence of fibrin, Centrifuging serum samples before a those from patients receiving

Volume Required: 10 µL serum.

assayed after extended storage. at -20°C or colder if samples are to be Storage: Stable at 2-8°C for 24 hours?

Warnings and Precautions

For in vitro diagnostic use.

accordance with applicable laws. Reagents: Store at 2-8°C. Dispose of in

B surface antigen; and for antibodies to materials derived from human blood were transmitting infectious agents. Source for antibodies to HIV 1 and 2; for hepatitis tested and found nonreactive for syphilis; all components as if capable of Follow universal precautions, and handle hepatitis C.

potentially explosive metal azides in lead preservative. On disposal, flush with large and copper plumbing. volumes of water to prevent the buildup of 0.1 g/dL, has been added as a Sodium azide, at concentrations less than

> sunlight. (See insert.) contamination and exposure to direct Chemiluminescent Substrate: Avoid

Water: Use distilled or deionized water.

Materials Supplied

barcode labels are needed for the assay. Components are a matched set. The

With barcode. 200 beads, coated with polyclonal goat anti-PSA antibody, with PSA Bead Pack (L2PS12) desiccant. Stable at 2-8°C until expiration

L2KPS2: 1 pack. L2KPS6: 3 packs.

after opening when stored as indicated. Store capped and reingerated: Stable at PSA antibody in buffer, with preservative PSA Reagent Wedge (L2PSA2) Recommended usage is within 30 days 2-8°C until expiration date. conjugated to monoclonal murine anti-Phosphatase (bovine call intestine) With barcode, 11.5 mL alkaline

of wedge; snap the sliding cover down into barcode. Remove the foil seal from the top the perforations, without damaging the Before use, tear off the top of the label at the ramps on the reagent lid. L2KP\$2: 1 wedge. L2KP\$6: 3 wedges.

Preservative. Stable at 2-8°C for 30 days PSA in a chicken serum/ouffer matrix, with PSA Adjustors (LPSL LPSH) Two vials (Low and High) 1.5 mL each of

L2KP\$2: 1 set. L2KP\$6: 2 sets.

after opening, or for 6 months (aliquotted)

can be read by the on-board reader. the kit) on test tubes so that the barcodes appropriate Aliquot Labels (supplied with Before making an adjustment, place the

Supplied Separately Kit Components

Storage: 30 days (after opening) at 2-8°C or 6 months (aliquotted) at -20°C. L2M2Z: 25 mL L2M2Z4: 55 mL protein/buffer matrix, with preservative. concentrated (ready-to-use), nonhuman One vial with barcode containing For the on-board dilution of high samples. Multi-Diluent 2 (L2M2Z, L2M2Z4)

L2PWSM: Probe Wash L2KPM: Probe Cleaning Kit L2SUBM: Chemiluminescent Substrate L2RXT: Reaction Tubes (disposable)

TMCO: Tri-level, multi-constituent control Also Required

Distilled or deionized water; test tubes;

Assay Procedure

adjustment assay, and quality control Manual for: preparation, setup, dilutions, See the IMMULITE 2000 Operator's procedures.

Adjustment Interval: 4 weeks.

Quality Control Samples: Use controls or sample pools with at least two levels (low and high) of PSA.

of Prostate Cancer **Expected Values in Detection**

samples were collected from 477 men, for prostate cancer detection purposes, other and 2 (<1%) provided no ethnic aged 50 or older. Of these, 20 (4%) were In a retrospective study at one clinical site Asian; 8 (2%) were African American; 440 digital rectal examination (DRE). Of these information. All patients also underwent (92%) were Caucasian; 7 (<1%) were 52 were biopsied for elevated

(> 4.0 ng/mL) PSA and/or suspicious DRE. The following table summarizes these clinical studies:

11.3%	ድ	DRE +	Ki	70	PSA > 4.0	477	All Subjects	E G
31.5%	17		54.3%	æ		ĸ	5	Popular E a
	œ			15		18		No. of Prostate Cancers
(25.3%-72.2%)	47.1%		(24.0%-55.7%)	39.5%		34.6%		% Positive Biopsies (95% CI)

(0.3%-48.3%		2.4%	78.8%
. 11.1%	-	ø	376
		DRE -	PSA <= 4.0 DRE -
(18.0%-54.2%		55.3%	9.9%
34.6%	φ	26	47
		DRE -	PSA > 4.0 DRE -
(7.6%-81.1%)		16.1%	6.5%
40.0%	N	(J	31
		DRE+	PSA <= 4.0 DRE +
(23.6%-76.4%)		52.2%	4.8%
50.0%	ø	12	23
		DRE +	PSA > 4.0 DRE +
% Positive Biopsies (95% CI)	Cancers	3	3
!		8	2 0

than DRE alone. PSA determinations more effective in detecting prostate cancer when used in conjunction with DRE, was even if the DRE is negative. However, the detected 50% (9/18) of cancers that DRE The study demonstrated that PSA testing 4 ng/mL may warrant additional testing did not; PSA elevations greater than suspicious DRE and a normal PSA may converse is also true: a subject with determinations did not. detected 11% (2/18) of cancers that PSA also require additional testing since DRE

identified as asymptomatic subjects. The In the same study, 376 participants were who had both a negative PSA and DRE PSA values by age decade for these following table contains the distribution of of prostate disease. Therefore, these data as for those subjects who were negative and therefore, were not biopsied as well asymptomatic subjects in the clinical study is questionable whether these subjects should be interpreted with caution since it that all of these subjects were indeed free for cancer biopsy. There is no certainty of age-specific reference ranges are safe represent a truly normal population. There are presently no data proving that the use

≥70 age group	60-69 age group	50-59 age group	All subjects	Distribution of PSA Levels
74	143	159	376	3
1.17	0.91	0.60	0.78	Median PSA
3.17	2.84	2.30	2.98	95 SA %II

261

Female Subjects	Number of Subjects / Samples
bjects	2 C
	0-4 4-10 10-20 20-40 >40 rg/ml ng/ml ng/ml ng/ml
	4-10 10-20 20-40 ng/mL ng/mL
	9 P
ŀ	9 ¥

Malignant Diseases	Nonmalignant Diseases 28/28 100% 0%	Healthy 149/149	253/253 100°
Diseases	ant Diseases	100% 0%	35
-	9 8	9%	9%
	3.	3	3
	Ş	3	3
			0

4731473 00 10 000	Healthy Male Subjects	78/78 100	The section of the se
È	bjec	×	9
	.	3	
!		100% 0% 0% 0% 0%	
•		3	
	-	3	

P	548/548	Non-Maligi	473/473
	548/548 78.2% 19.3% 3.5% 0.9% 0%	Non-Malignant Diseases	473/473 99.4% 0.6% 0% 0% 0%
	3.5%		ş
	0.9%		Ş
	3		3

68/66	Other Pros	333/333	BPH
80.3% 18.2% 1 Ev ~	Other Prostatic Diseases	333/333 67.9% 25.8% 5.4% 0.9% 0%	
E		5.4%	
}		0.9%	
!		Ş	

Other Nonprostatic Diseases	66/66 80.3%	Carolin Colaire Diseases
Ö.	18.29	Seere
202	80.3% 18.2% 1.5%	
ļ	3	
	Ş	

Droatete Constitution of	312/312 93.0% 6.1% 0.6% 0.3%	Non-Prostatic Malignancies
	9,000	2
	0.3%	
ı	Ş	

274/274	
	: Carrie Carrow (single specimens)
21.2% 13.	ingle spec
42.3% 21.2% 13.1% 7.3% 16.	imens)
16.19	

5/758	Ca Ca	
54.8% 11.7% 10.7% 7.5% 15.3%	tate Cancer (serially monitored)	15.1% 75.3% 21.6% 13.1% 7.3% 16.1%
15.3%		16.1%

7708

Median 95" %ile
- 1
0.60 2.30
0.91 2.84
7 3.17
0.78 0.78 0.80

istudy.	lents were tested. Shown below is the	8 samples collected from 1965	studies performed at four clinical sites.
OI IM	ere tesi	Ses col	perform
WOLLE	ed. Sh	ected	ned at f
PSA	OWn be	from 1	our clir
results	ej Mole	965	Ji Cel Si
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naie Subjects	ber of
Cia	10 P
i	0-4 4-10 10-20 20-40 >40 ng/ml ng/ml ng/ml ng/ml ng/ml ng/ml
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mare adojects	Jecus				
253/253	100% 0%	3	3	3	3
ealthy					1
149/149 100% 0%	ĩ 0 0%	9%	Ş	3	3
Vonmalignant Diseases	ant Dise	8.585			

78/78	Malignant Diseases	28/28	Nonmalignant Diseases	149/149 100% 0%
100% 0%	Diseases	100% 0%	uant Dise	100%
3	_	3	8505	3
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473/473	Healthy Male Subjects
473/473 99.4% 0.6% 0%	Subjects
ş	İ
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13	- 1

Other No.	68/66	
Other Nonprostatic Diseases	80.3% 18.2% 1.5%	Control Control Control
58	6 1.5%	
	3	

7-Prostatic Malionanciae	49/149 93.2% 5.4% 0%	ther Nonprostatic Diseases
tic Mali	93.2%	prostatic
	5.4%	Disease
5	ş	3
	1.3%	
	3	

274/274 42.3% 21.2% 13.1% 7.3% 16	(Value Cancer (single specimens)
<u>.</u>	

105/758	
54.8% 11.7% 10.7% 7.5%	(Determination (Committee of the Committee of the Committ
35.33 39	

tion of	5	PSA Median	PSA PSA	Number of
CLS	376	0.78	2.98	Samples
group	159	0.80	2.30	Stage A
ge group	ž	0.91	2.84	17/174
group	74	1.17	3.17	Stage B
				31/200

nts were tested. Shown below is the oution of IMMULITE PSA results from tudy.	dies performed at four clinical sites, samples collected from 1965
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Stage C

19/102

56.9% 6.9% 7.8% 8.8% 19.6%

13.1% 11.7% 8.9% 18.0%

31/200

54.0% 14%

12% 8.5% 11.5%

64.9% 9.8% 9.2% 3.5% 12.6%

nymt nymt nymt nymt nymt

10 10-20 20-40

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?

Stage D

!	0-20 20-40 >40 or ng/ml		
Consider these lin	1965/2618 1962	Total:	38/282
.`` ` 0 80 ±	1962		48.2%

275

138

8

ź

reference ranges. Consider these limits as guidelines only. Each laboratory should establish its own

Limitations

disease, nor should serum PSA be used presence or absence of malignant interpreted as absolute evidence for the Serum PSA concentrations should not be alone as a screening test for malignant disease."

Prediction of malignant prostatic disease which may also include serial serum PSA complete clinical evaluation of the patient recurrence should be based on a determinations.

prostate gland may lead to elevated PSA levels persisting up to 3 weeks. 18 massage, since manipulation of the biopsy, prostatectomy or prostatic Samples should be obtained before

adequately reflect the presence of residual or recurrent disease. 25 includes hormonal therapy may not a prostatic cancer treatment which Consequently, a low PSA result following PSA expression may be altered due to normonal therapy for prostate cancer.

specimens from patients who have antibodies derived from mice. In particular, may show emoneous results in such antibodies (HAMA). These specimens therapy may contain human anti-mouse received preparations of mouse interference in immunoassays that employ mouse protein which can cause Some individuals have amboodies to monoclonal antibodies for diagnosis or

IMMULITE 2000 PSA

IMMULITE 2000 PSA

assays. 2014 Therefore, results should be interpreted with caution for such patients Heterophilic antibodies in human serum

exposed to animals or animal serum 33.) Samples from patients routinely antibodies: a problem for all [See Boscato LM, Stuart MC. Heterophilic included in the assay components causing can react with the immunoglobulins combination with the clinical examination, components can occur. For diagnostic purposes, the results obtained from this interference potentially causing an products can demonstrate this type of immunoessays. Clin Chem 1988:34:27interference with in vitro immunoassays. been formulated to minimize the risk of anomalous result. These reagents have patient medical history, and other findings assay should always be used in interactions between rare sera and test interference; however, potential

Performance Data

See Tables and Graphs for data impresentative of the assay's performance Results are expressed in right. (Unless otherwise noted, all were generated on serum samples collected in tubes without gel barriers or clot-promoting additives.)

Working Range: 0.04 - 150 ng/mL

Analytical Sensitivity: 0.04 ng/mL

High-dose Hook Effect: None up to 22,500 ng/mL

Precision: Samples were processed in duplicate over the course of 20 days, two runs per day, for a total of 40 runs and 80 replicates. Results are expressed in ng/mL

		Withi	Within-Run	, o	Total
	Mean	So	CV	SD CV	১
-	2.8	0.10	3.6%	0.14 5.0%	5.0%
N	7.4	0.23	3.1%	0.36	¥6.¥
ω	11.4	0.34	3.0%	0.60 5.3%	5.3%
•	ß	0.70	0.70 2.8%	=	4.4%
U	g	7	2.2%	2.5	3.9%
B	126	3.2	2.5%	4.7	1.7 3.7%

Linearity: Samples were assayed under various dilutions. Results are expressed in ng/mL.

ı				(J)	l				•	l				ω	1				N						
1 in 16	2 in 16	4 in 16	8 in 16	16 in 16	1 in 16	2 in 16	4 in 16	œ 5 6	16 in 16	1 m 16	2 in 16	4 in 16	8 m 16	16 in 16	1 m 16	2 in 16	4 in 16	8 in 16	16 in 16	1 in 16	2 in 16	4 in 16	8 5 6	16 in 16 ⁵	Dilution
8.9	17	ස	61	126	6.7	13	25	*	8	1.7	3.6	7.0	13.9	27.2	0.51	0.98	2.05	3.96	7.8	0.06	0.13	0.23	0.48	1.03	Observed
7.9	5	೫	ස	ı	6.2	ฆ	25	8	ı	1.7	3.4	6.8	13.6	ı	0.49	0.98	1.95	3.90	1	0.06	0.13	0.26	0.52	1	Expected
113%	106%	103%	97%	1	108%	108%	100%	96%	I	100%	106%	103%	102%	1	105%	100%	105%	101%	ı	100%	100%	91%	92%	1	%O/E

Recovery: Samples spiked 1 to 19 with four PSA solutions (107, 208, 653 and 817 ng/mL) were assayed. Results are expressed in ng/mL.

				ω					N					-	
0	ဂ	œ	>	ı	0	O	œ	>	l	0	ဂ	Φ	>	ı	Solution
S.	8	x	28	8	49	\$	5	11.8	6.4	4 5	ಜ	11.2	6.0	0.48	Observed
8	88	35	ઝ	l	47	39	17	11.5	١	*	ಜ	10.8	5.8	i	Expected
98%	97%	91%	93%	i	104%	108%	94%	103%	ı	102%	100%	104%	103%	1	%O/E

Bilirubin: No significant effect.
Hemotysis: No significant effect

Specificity: The assay is highly specific for prostate-specific antigen, with a particularly low crossreactivity to other naturally occurring compounds and chemotherapeutic agents that might be present in patient samples.

Percent

ND: not detectable

Samples used were within the working using Deming regression analysis. nonisotopic PSA assays were compared Method Comparison: All four of DPC's range of the assays. The table below

> presents the results of the Deming regressions, with columns as Y, and rows

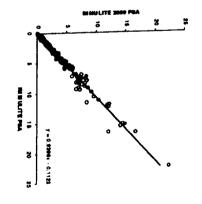
Results of Deming Regressions

IM 3rd (MULIT Genera	E 2000 Mion P	SA	3rd (IMMU Genera	LITE	SA	IMMI	JLITE	2000 F	PSA		IMULI1	re PS/	•	
Commission Coefficient	intercept (95% CI)	Stope (95% CI)	5	Consistion Coefficient	Intercept (95% CI)	Slope (95% CI)	3	Completion Coefficient	(95% CI)	Stope (95% Ct)	>	Combaton Coefficient	Intercept (95% CI)	(95% CI)	3	1
0.991	-0.06 (-0.10 to -0.02)	0.92 (0.91 to 0.94)	473	0.993	-0.06 (-0.09 to -0.02)	1.01 (1.00 to 1.03)	474	0.992	0.12 (0.08 to 0.16)	1.06 (1.05 to 1.08)	477					PSA PSA
0.990	-0.16 (-0.20 to -0.12)	0.86 (0.85 to 0.87)	473	0.988	-0.15 (-0.19 to -0.10)	0.94 (0.93 to 0.96)	474					0.992	-0.11 (-0.15 to -0.07)	0.94 (0.93 to 0.95)	477	IMMULITE 2000 PSA
0.990	0.00 (-0.04 to 0.04)	0.91 (0.90 to 0.92)	472					0.988	0.15 (0.11 to 0.20)	1.06 (1.05 to 1.08)	474	0.993	0.05 (0.02 to 0.09)	0.99 (0.98 to 1.00)	474	IMMULITE 3rd Generation PSA
				0.990	-0.00 (-0.05 to 0.05)	1.10 (1.09 to 1.11)	472	0.990	0.18 (0.14 to 0.23)	1.16 (1.14 to 1.17)	473	0.991	0.06 (0.02 to 0.11)	1.08 (1.07 to 1.10)	473	IMMULITE 2000 3rd Generation PSA

PSA and IMMULITE PSA on 477 patient The following graph presents the comparison between IMMULITE 2000 (IML 2000) = 0.94 (IML) - 0.11 ng/ml nondetectable to approximately samples. (Concentration range: 20 ng/mL.) By linear regression:

2.30 ng/mL (IMMULITE 2000)

r = 0.992



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Technical Assistance

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or the collection of diagnostic blood specimens

Technical Services department In the United States, contact DPC's

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Fax: 973.927.4101. Outside the United
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Diagnostic Products Corporation 5700 West 98th Street Los Angeles CA 90045-5597 2001-05-01 (ISO 8601) May 1, 2001 PIL2KPS - 4

Third Generation PSA

Third Generation PSA IMMULITE 2000

English

the quantitative measurement of prostate with the IMMULITE 2000 Analyzer - for an aid in the detection of prostate cancer specific antigen (PSA) in human serum, as Intended Use: For in vitro diagnostic use or older. This assay is further indicated as examination (DRE) in men aged 50 years when used in conjunction with digital recta an adjunctive test to aid in the

Catalog Number: L2KUP2 (200 tests) management of prostate cancer patients

L2KUP6 (600 tests)

Test Code: sPs Color: Red

Caution: In the United States, Federal law restricts this device to sale by or on the order of a physician.

assays can vary due to differences in specificity. The results reported by the assay methods and reagent specimen determined with different The concentration of PSA in a given Values obtained with different PSA include the identity of the assay used. serially monitored. the baseline values for patients being assays, the laboratory must confirm interchangeably. Before changing laboratory to the physician must assays cannot be used

Summary and Explanation

it contains approximately 10% carbohydrate by weight.¹² The amino acid sequence of PSA was reported,³ and the gene has been cloned.⁴ PSA is in 1979, is a glycoprotein monomer with protesse activity. 12 PSA has an isoelectric identified and characterized by Wang, et al Prostate specific antigen (PSA), first weight of approximately 33-34 kilodaltons; point of approximately 6.9 and a molecular phosphatase activity. from PAP and does not exhibit enzymatic biochemically and immunologically distinct

> prostatic ductal epithelium and in PSA is localized in the cytoplasm of it can be recovered and purified both from PSA is a secretory protein of the prostate, secretions of the ductal lumina. Because prostatic tissue and from seminal plasma PSA has been found to be exclusively nonprostatic carcinoma, healthy women or women with cancer. 5.8 tissues, but not in healthy men, men with conditions of other adjacent genitourinary prostatic hypertrophy, and inflammatory patients with prostate cancer, benign elevated serum PSA has been found in associated with prostate tissue," and

suitable as a screen for prostate cancer Measurement of serum PSA is not prostatic hypertrophy (BPH)*; nor is it ultrasonography in the event of abnormal measurement and rectal examination with staging. The combination of PSA also observed in patients with benign because elevated PSA concentrations are offers several advantages over digital examination alone. Measurement of PSA detecting prostate cancer than rectal findings may provide a better method of recommended as a guide in disease objective, quantitative, and obtained rectal examination or ultrasonography in the procedure is more acceptable to independent of the examiner's skill, and detecting prostate cancer: the result is patients than other procedures.*

PSA can be useful in detecting metastatic Determinations of total immunoreactive or persistent disease in patients following indicative of recurrent or residual disease. 12-16 Hence, PSA is widely pretreatment PSA concentrations is following treatment or an increase in the cancer.16,11 Persistent elevation of PSA surgical or medical treatment of prostate accepted as an aid in the management of prostate cancer patients. 12-16

men who have at least a 10-year life offered annually, beginning at age 50, to The American Cancer Society has expectancy, as well as younger men who test and digital rectal examination be recommended that both the PSA blood

> with two or more affected first-degree relatives may consider screening at a younger age, perhaps 45.27 Men in high risks groups, such as those benefits of early detection and treatment information regarding potential risks and are at high risk. Patients should be given

Incubation Cycles: 2 × 30 minutes Sequential Immunometric Assay. Principle of the Procedure

Specimen Collection

massage, since manipulation of the PSA level using conventional PSA assays. 19.20 Therefore, when possible, of an effect of digital rectal examination or shown conflicting results on the existence levels persisting for up to 3 weeks using conventional PSA assays. ** Studies have prostate gland may lead to elevated PSA biopsy, prostatectomy or prostatic Samples should be obtained before obtain PSA samples before digital rectal examination.

presence of fibrin. To prevent erroneous complete clot forms may result in the Centrifuging serum samples before a samples. Some samples, particularly ensure that complete clot formation has results due to the presence of fibrin, increased clotting time. anticoagulant therapy, may require those from patients receiving taken place prior to centrifugation of

Volume Required: 50 µL serum.

be assayed after extended storage. Store at -18°C or colder if samples are to Storage: 24 hours at 2_8°C.21

For in vitro diagnostic use. Warnings and Precautions

accordance with applicable laws. Reagents: Store at 2-8°C. Dispose of in

B surface antigen; and for antibodies to materials derived from human blood were transmitting infectious agents. Source all components as if capable of Follow universal precautions, and handle for antibodies to HIV 1 and 2; for hepatitis tested and found nonreactive for syphilis;

> volumes of water to prevent the buildup of potentially explosive metal azides in lead 0.1 g/dL, has been added as a Sodium azide, at concentrations less than and copper plumbing. preservative. On disposal, flush with large

sunlight. (See insert.) contamination and exposure to direct Chemiluminescent Substrate: Avoid

Water: Use distilled or deionized water.

Materials Supplied

barcode labels are needed for the assay. Components are a matched set. The

Third Generation PSA Bead Pack

Monoclonal murine arti-PSA artibody. Stable at 2-8°C until expiration date. L2KUP2: 1 pack. L2KUP6: 3 packs. With barcode, 200 beads, coated with

(L2UPA2) Third Generation PSA Reagent Wedge

intestine) conjugated to polyclonal goat anti-PSA antibody in buffer, with preservative. Stable at 2-8°C until expiration date. 11.5 mL alkaline phosphatase (bovine call buffer/serum matrix, with preservative. With beroode, 11.5 mL of a protein

of wedge; snap the sliding cover down into barcode. Remove the foil seal from the top the perforations, without damaging the Before use, tear off the top of the label at the ramps on the reagent lid. L2KUP2: 1 wedge. L2KUP6: 3 wedges

Third Generation PSA Adjustors (LUPL

PSA in a serum matrix, with preservative. Stable at 2-8°C for 30 days after opening. or for 6 months (aliquotted) at -20°C. Two vials (Low and High), 3 mL each, of L2KUP2: 1 set L2KUP6: 2 sets.

appropriate Aliquot Labels (supplied with Before making an adjustment, place the can be read by the on-board reader. the kit) on test tubes so that the barcodes

Supplied Separately Kit Components

One vial with barcode containing For the on-board dilution of high samples protein/buffer matrix, with preservative. concentrated (ready-to-use), nonhuman Multi-Diluent 2 (L2M2Z, L2M2Z4) or 6 months (aliquotted) at -20°(Storage: 30 days (after opening) at 2-8°C L2M2Z: 25 mL. L2M2Z4: 55 mL

L2SUBM: Chemiluminescent Substrate L2KPM: Probe Cleaning Kit L2PWSM: Probe Wash

LUPCM: Single-level Third Generation L2RXT: Reaction Tubes (disposable) TMCO: Tri-level, multi-constituent control

Distilled or deionized water; test tubes; Also Required PSA Control Module

Assay Procedure

See the IMMULITE 2000 Operator's adjustment, assay and quality control Manual for: preparation, setup, dilutions

Adjustment interval: 4 weeks.

or sample pools with at least two levels Quality Control Samples: Use controls (low and high) of PSA.

of Prostate Cancer **Expected Values in Detection**

In a retrospective study at one clinical site other and 2 (<1%) provided no ethnic (92%) were Caucasian; 7 (<1%) were aged 50 or older. Of these, 20 (4%) were samples were collected from 477 men, for prostate cancer detection purposes, information. All patients also underwent Asian; 8 (2%) were African American; 440 digital rectal examination (DRE). Of these, 52 were biopsied for elevated

these clinical studies: DRE. The following table summarizes (> 4.0 ng/mL) PSA and/or suspicious

477	All Subject	E co
æ	5	Biopsis
ī.		No. of Prostate Cancers
34.6%		% Positive Biopsi (95% CI)

76.1%	363	PSA <= 4.0	12.6%	8	PSA > 4.0	6.1% %	8	PSA <= 4.0	5.2%	25	PSA > 4.0	11.3%	ድ	DRE +	17.8%	85	PSA > 4.0	×	No. 9
0.8%	ω	O DRE -	53.3%	×	DRE -	13.8%	•	DRE +	52.0%	13	DRE +	31.5%	17		52.9%	\$		2	3 8
	-			ø			_			7			00			ő		Cancers	
(0.8%-90.6%)	33.3%		(15.2%-48.2%)	28.1%		(1.3%-75.1%)	25.0%		(28.0%-77.6%)	53.8%		(25.3%-72.2%)	47.1%		(22.8%-51.2%)	35.6%		% Positive Biopsies (95% CI)	

more effective in detecting prostate cancer than DRE alone. PSA determinations when used in conjunction with DRE, was did not; PSA elevations greater than detected 50% (9/18) of cancers that DRE The study demonstrated that PSA testing, suspicious DRE and a normal PSA may even if the DRE is negative. However, the 4 ng/mL may warrant additional testing detected 6% (1/18) of cancers that PSA also require additional testing since DRE converse is also true: a subject with determinations did not

In the same study, 363 participants were PSA values by age decade for these identified as asymptomatic subjects. The and therefore, were not biopsied as well who had both a negative PSA and DRE asymptomatic subjects in the clinical study following table contains the distribution of of prostate disease. Therefore, these data as for those subjects who were negative should be interpreted with caution since it is questionable whether these subjects that all of these subjects were indeed free for cancer biopsy. There is no certainty represent a truly normal population. There are presently no data proving that the use

Prostate Cancer (single specimens)

93.0% 6.1% 0.6% 0.3%

ş

Prostate Cancer (serially monitored) 105/758 54.8% 11.7% 10.7% 7.5%

42.3% 21.2% 13.1% 7.3%

of age-specific reference ranges are safe or effective.

≥70 age group	60-69 age group	50-59 age group	All subjects	Distribution of PSA Levels
69	137	157	383	5
. .	1.12	0.88	1.02	PSA Median
358	3.15	2.83	3.20	PSA 95 th %ile

distribution of IMMULITE PSA results from patients were tested. Shown below is the 2618 samples collected from 1965 In studies performed at four clinical sites, this study.

Non-Prostatic Mailgnancies	149/149	Other Nonprostatic Diseases	88/88	Other Prostatic Diseases	333/333	ВРН	548/548	Non-Malignant Disc	473/473	Healthy Male Subjects	76/76	Malignant Diseases	28/28	Nonmalignant Diseases	149/149	Healthy	253/253	Female Subjects	Number of Subjects / Samples
ic Mai	93.2%	prostatio	80.3%	tatic Dis	67.9%		78.2%		93.4%	le Subj	8)isease	100%	Int Disa	100 ×		8	ects	
gnanci	5.4%	Diseas	80.3% 18.2%	10388	67.9% 25.8%		76.2% 19.3%		0.6%	S.	ş		3	3508	%		9		10 10 10
3	3	ž	1.5%		5.4%		3.5%		3		Ş		3		9%		Ş		70-20 70-20
	1.3%		3		0.9%		0.9%		Ş		3		Ş		Ş		Ş		3 6
	9		ş		9		3		ş		Ş		3		3		3	ŀ	3 4

Number of Subjects / Samples Total: Stage D Stage C Stage B Stage A 1965/2618 1962 38/282 19/102 31/200 64.9% 9.8% 48.2% 13.1% 11.7% 8.9% 18.0% 58.9% 6.9% 7.8% 8.8% 19.6% 54.0% 14% <u>۽</u> 1 10 10-20 20-40 mg/mt ng/mt ng/mt ng/mt ng/mt ng/mt 275 9.2% 3.5% 12.6% 12% 8.5% 11.5% <u>ឆ</u> 8 30/11/20 ઠ ğ

reference ranges. Each laboratory should establish its own Consider these limits as guidelines only

presence or absence of malignant interpreted as absolute evidence for the Serum PSA concentrations should not be disease.

complete clinical evaluation of the patient recurrence should be based on a Prediction of malignant prostatic disease determinations. which may also include serial serum PSA

biopsy, prostatectomy or prostatic massage Samples should be obtained before

PSA expression may be aftered due to

early detection of prostate cancer. reflect the presence of residual or recurrent disease.28 Consequently, a low PSA result following hormonal treatment may not adequately hormonal therapy for prostate cancer. This device is not intended to be used for

may show erroneous results in such assays. 22 Therefore, results should be specimens from patients who have antibodies derived from mice. In particular interpreted with caution for such patients therapy may contain human anti-mouse monocional antibodies for diagnosis or interference in immunoassays that employ mouse protein which can cause Some individuals have antibodies to antibodies (HAMA). These specimens received preparations of mouse

15.3%

can react with the immunoglobulins immunoassays. Clin Chem 1988:34:27antibodies: a problem for all [See Boscato LM, Stuart MC. Heterophilic interference with in vitro immunoassays. included in the assay components causing Heterophilic antibodies in human serum interference potentially causing an anomalous result. These reagents have products can demonstrate this type of exposed to animals or animal serum Samples from patients routinely purposes, the results obtained from this components can occur. For diagnostic interactions between rare sera and test been formulated to minimize the risk of terference; however, potential

Performance Data

patient medical history, and other findings combination with the clinical examination,

assay should always be used in

otherwise noted, all were generated on See Tables and Graphs for data serum samples collected in tubes without gel barriers or clot-promoting additives.) Results are expressed in ng/mL. (Unless epresentative of the assay's performance

Calibration Range: Up to 20 ng/mL

Analytical Sensitivity: 0.003 ng/mL

Functional Sensitivity: 0.01 ng/mL, as concentration that can be measured with sensitivity is defined as the lowest in the Precision section. (Functional demonstrated by the studies summarized an interassay CV of 20%.)

None up to 112,000 ng/ml.. High-dose Hook Effect:

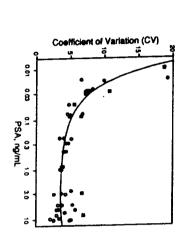
replicates. Results are expressed in runs per day, for a total of 40 runs and 80 duplicate over the course of 20 days, two Japan. Precision: Samples were assayed in

		UNY-UNITARY		1003	B
	Mean	SD	CV	S	۲
-	0.028	0.002	7.1%	0.003	10.7%
N	3.0	0.11	3.7%	0.20	6.7%
ယ	8.3	0.25	3.0%	0.57	6.9%

concentration pools, prepared from A second study included lowunspiked patient samples

		Within-Bug	Buo	Total	
l	Mean	SD	C۷	SD	CV
_	0.0067	0.0067 0.00136 20.3% 0.00141	20.3%	0.00141	21.0%
N	0.0098	0.0098 0.00183 18.7% 0.00183	18.7%	0.00183	18.7%
ω	0.027	0.0020	7.3%	0.0021	7.8%
4	0.050	0.0024	4.8%	0.0028	5.6%
Ç	0.086	0.0042	4.9%	0.0056	6.5%
6	0.294	0.0129	4.4%	0.0134	4.6%
7	0.430	0.0173	4.0%	0.0183	4.3%
00	0.861	0.0321	3.7%	0.0334	3.9%

CVs from three Master Curve studies, 10 Precision Profile: Based on within-run shaped contour line traces the or 20 replicates per sample, in addition to circles). For reference, the run-to-run the within-run CVs tabulated. The bowlsquares approximate path of these points (open ("total") CVs tabulated are plotted as solid



Linearity: Samples were assayed under

																				ı
			(J)				4				ω	ĺ			N				-	
1 in 8	2 in 8	4 in 8	8 in 8	1 in 8	2 in 8	4 in 8	8 n 8	1 in 8	2 in 8	4 in 8	& 5 0	1 in 8	2 5 8	4 in 8	8 5 8	1 in 8	2 in 8	4 5 8	8 5 8	Dilution
2.1	1.	œ œ	17.7	1.5	3.0	6.1	12.3	0.81	1.7	3.3	6.5	0.17	0.38	0.73	1.5	0.014	0.026	0.054	0.109	Observed
2.2	:	8.9	ı	1.5	3.1	Ø. 23	ì	0.81	1.6	3.2	ı	0.19	0.38	0.75	ł	0.014	0.027	0.055	ŀ	Expected
95%	100%	99%	ı	100%	97%	%86	ŀ	100%	106%	101%	1	89%	100%	97%	1	100%	96%	98%	1	%O/E

Specificity: The antibody is highly specific

ND: not detectable.	Prolactin	PAP	HCG	Ferritin .	CEA	AFP	Compound
, the state of the	200 ng/mL	1000 ng/mL	100000 mlU/mL	10000 ng/mL	100 ng/mL	10000 ng/mL	Amount Added
	NO.	N D	8	S	8	8	% Cross- reactivity

various dilutions. Results are expressed in

Dilution	Observed	Expected	%O/E
8 in 8	0.109	ŀ	1
4 in 8	0.054	0.055	98%
2 in 8	0.026	0.027	96%
1 in 8	0.014	0.014	100%
89 57 89	. 5	ı	ŀ
4 5 8	0.73	0.75	97%
2 in 8	0.38	0.38	100%
1 in 8	0.17	0.19	89%
8 5	6.5	ı	l
4 in 8	3.3	3.2	101%
2 in 8	1.7	1.6	106%
1 in 8	0.81	0.81	100% *
\$ in 8	12.3	ł	ł
4 in 8	ъ Э	Ø. N	98%
2 5 8	3.0	3.1	97%
1 in 8	1.5	1.5	100%
5 8 in 8	17.7	ı	ı
4 in 8	8.8	8.9	99%
2 in 8	:	‡	100%
1 in 8	2.1	2.2	95%

Bilirubin: No significant effect.

O

18

5

95%

Hemolysis: No significant effect

three PSA solutions (10.2, 48 and 91 ng/mL) were assayed. Results are expressed in ng/mL. Recovery: Samples spiked 1 to 19 with

			os.	ı			(Ji				4				ω				N						4
,	0 0	>	i	ဂ	B	>	i	c	00	>	ı	c	œ	>	ŀ	C	œ	>	ı	c	œ	>	1	Spiking Solution	00000
•	17	17	1 6	160	i de	17	5	12	=	8.9	9.1	=	9.6	9.0	8.3	5.2	3.6	2.5	1.7	4.7	2.8	1.8	0.87	Observed	
5	17	17	1	19	17	17	1	ಪ	=	9.6	ı	īž	9.9	8.8	ŀ	5.8	3.6	2.6	1	5.0	2.8	. .	ı	Expected	
2	106%	100%	ı	100%	106%	100%	i	92%	100%	93%	1	92%	97%	102%	1	90%	100%	96%	1	94%	100%	100%	1	%O/E	

Samples used were within the working using Deming regression analysis. nonisotopic PSA assays were compared Method Comparison: All four of DPC's

presents the results of the Deming regressions, with columns as Y, and rows range of the assays. The table below

MMULTE

Results of Deming Regressions

310	MMUL d Gene	ITE 20		310	IMM I Gene	ULITE	PSA	IMA	MULITE	2000	PSA	.	MMUL	ITE P	SA	
Coefficient	(95% C)	(95% CI)	2	Coefficient	(36% CI)	(95% CI)	?	Coefficient	(95% CI)	(95% CI)	2	Coefficient	(95% CI)	(95% CI)	2 3	ר
0.991	-0.06 (-0.10 to -0.02)	0.92 (0.91 to 0.94)	473	0.993	-0.08 (-0.09 to -0.02)	1.01 (1.00 to 1.03)	474	0.992	0.12 (0.08 to 0.16)	1.06 (1.05 to 1.08)	477					IMMULITE PSA
0.990	-0.16 (-0.20 to -0.12)	0.86 (0.85 to 0.87)	473	0.988	-0.15 (-0.19 to -0.10)	0.94 (0.93 to 0.98)	474					0.992	(-0.15 to -0.07)	0.94 (0.93 to 0.95)	477	IMMULITE 2000 PSA
0.990	0.00 (- 0.04 to 0.04)	0.91 (0.90 to 0.92)	472					0.986	0.15 (0.11 to 0.20)	1.06 (1.05 to 1.08)	474	0.993	0.05 (0.02 to 0.09)	0.99 (0.98 to 1.00)	474	3rd Generation PSA
				0.990	-0.00 (-0.05 to 0.05)	1.10 (1.09 to 1.11)	472	0.990	0.18 (0.14 to 0.23)	1.16 (1.14 to 1.17)	473	0.991	0.06 (0.02 to 0.11)	1.08 (1.07 to 1.10)	473	IMMULITE 2000 3rd Generation PSA

The following graph presents the comparison between IMMULITE 2000 Third Generation PSA and IMMULITE approximately 20 ng/mL. See graph.) By (Concentration range: nondetectable to Third Generation PSA on 472 samples. linear regression:

PSA) - 0.00 ng/mL (IML 2000 3" Gen. PSA) = 1.10 (IML 3" Gen

2.34 ng/mL (IMIL 2000) 2.16 ng/mL (IMIL)

-0.98

P# y + 1 00041 - 0 0000

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> polyclonal immunoassay compared. Clin Chem of carcincembryonic arrigen in patients receiving murine antibody for degrees and therapy. Clin Chem 1968;24:261-4, 23) Hansen HJ, et al. Solving the problem of antibody interference in commercial "sandwich" type marker for adenocarcinoma of the prostate. J critical assessment of the most useful tumor Cesterling JE. Prostate specific antigen: a prostatectomy. J Urol 1989;141:873-9, 16) determinations before and after radical 1967;33:1916-20, 15) Lange PH, et al. The value of serum prostate specific arrigen al. Serum prostatic apacific arrigan: in vitro stability and the effect of ultrasound rectal examination in vivo, Ann Clin Biochem effect of digital rectal examination on serum levels of prostatic specific antigen. Arch Pathol Lab Med 1988;112:1110-2, 20) Hughes HR, et andgen by the periurethral glands. J Urol 1993;149:783-6. 18) Stamey TA, Yang N, et al. evidence for secretion of prostate specific K, et al. An analysis of urinary prostate specific antigen before and after radical protatectomy: Urol 1991;145:907-23. 17) Iwakiri J, Grandbois ER, editors. Tietz textbook of clincal chemistry. 2nd ed. Philedelphia: W.B. Saunders, 1994, 22) Prostate specific antigen as a serum marker for Primus FJ, et al. "Sendwich"-type immunoassay 1967;317:509-16. 19) Brawer MK, et al. The adenocarcinoma of the prostate. N Engl J Med Human anti-murine immunoglobulin responses in patients receiving monoclonal ambody therapy. Cancer Res 1985;45:879-85. 25) 1987:24(Suppl):206-8, 21) Burtis CA, Ashwood immunoassay of carcinoembryonic antigen. Clin Chem 1969;35:146-51. 24) Schroff RJ, et al. adenocarcinoma of the prostate: impact of adjuvent treatment (hormonal and radiation). J values after radical retropubic prostatectomy for Morgan WR, et al. Prostate specific antigen antigen by a time-resolved immunofluorometric Ural 1991;145:319-23. 26) Ferguson RA, Yu H RA, et al. American Cancer Society guidelines for the early detection of cancer. CA Cancer J immunochemiluminascent third-generation Ultrasensitive detection of prostate-specific assay. Clin Chem 1996;42:675-84. 27) Smith BEERY and the IMMULITE Calyvas M. Zammit S, Diamandis EP.

Technical Assistance

Clin 2000; 50(1):34-49.

In the United States, contact DPC's Corporation is registered to ISO 9001:1994 The Quality System of Diagnostic Products States, contact your National Distributor Fax: 973.927.4101. Outside the United Technical Services department. Tel: 800.372.1782 or 973.927.2828

IMMULITE 2000 Third Generation PSA

MMULITE 2000 Third Generation PSA

Diagnostic Products Corporation 5700 West 96th Street Los Angeles, CA 90045-5597 2001-05-01 (ISO 8601)
May 1, 2001
PIL2KUP – 4

IMMULIIE PSA

English

quantitative measurement of prostatemanagement of prostate cancer patients or older. This assay is further indicated as examination (DRE) in men aged 50 years when used in conjunction with digital rectal an aid in the detection of prostate cancer specific arrigen (PSA) in human serum, as with the IMMULITE Analyzer - for the Intended Use: For in vitro diagnostic use an adjunctive test to aid in the

Catalog Number: LKPS1 (100 tests). LKPS5 (500 tests)

Test Code: PSA Color: Brown

restricts this device to sale by or on the Caution: In the United States, Federal law order of a physician.

the baseline values for patients being assays, the laboratory must confirm interchangeably. Before changing assays cannot be used Values obtained with different PSA include the identity of the assay used specificity. The results reported by the assay methods and reagent assays can vary due to differences in specimen determined with different The concentration of PSA in a given serially monitored laboratory to the physician must

containing approximately 10% carbohydrate by weight. 2 Subsequently in 1979 is a glycoprotein monomer with professe activity. 12 PSA has an isoelectric Summary and Explanation point of approximately 6.9 and a molecular Prostate specific antigen (PSA) first weight of approximately 33-34 kilodaltons identified and characterized by Wang et al PSA is biochemically and immunologically reported", and the gene has been cloned." the amino acid sequence of PSA was enzymatic phosphatase activity distinct from PAP and does not exhibit

PSA is localized in the cytoplasm of secretions of the ductal lumina. Because prostatic ductal epithelium and in

> PSA has been found to be primarily it can be recovered and punitied both from PSA is a secretory protein of the prostate, conditions of other adjacent genitourinary prostatic hypertrophy, and inflammatory patients with prostate cancer, benign elevated serum PSA has been found in associated with prostate tissue, and prostatic tissue and from seminal plasma. nonprostatic carcinoma, healthy women or women with cancer.5.8 tissues but not in healthy men, men with

observed in patients with benign prostatic hypertrophy (BPH), nor is it screen for prostate cancer because Serum PSA alone is not suitable as a staging. The combination of PSA elevated PSA concentrations are also ultrasonography in the event of abnormal measurement and rectal examination with recommended as a guide in disease the procedure is more acceptable to independent of the examiner's skill, and objective, quantitative, and obtained detecting prostate cancer: the result is rectal examination or ultrasonography in offers several advantages over digital examination alone. Measurement of PSA detecting prostate cancer than rectal findings may provide a better method of patients than other procedures."

in patients following surgical or medical treatment of prostate cancer. 10,11 PSA determinations can be useful in detecting metastatic or persistent disease indicative of recurrent or residual disease. 12-16 Hence PSA is widely pretreatment PSA concentrations is Persistent elevation of PSA following accepted as an aid in the management of prostate cancer patients. 12-18 Concurrent treatment or an increase in the measurement of PAP may contribute additional information. 17

offered annually, beginning at age 50, to test and digital rectal examination be men who have at least a 10-year life recommended that both the PSA blood benefits of early detection and treatment are at high risk. Patients should be given expectancy, as well as younger men who The American Cancer Society has Men in high risks groups, such as those information regarding potential risks and

IMMULITE PSA

relatives may consider screening at a younger age, perhaps 45.77 with two or more affected first-degree

Immunometric Assay. Principle of the Procedure

Incubation Cycles: 1 × 30 minutes.

Specimen Collection

prostate gland may lead to elevated PSA levels persisting for up to 3 weeks. massage, since manipulation of the biopsy, prostatectomy or prostatic Samples should be obtained before

the existence of an effect of digital rectal examination on PSA level. 1929 Therefore digital rectal examination. Studies have shown conflicting results on when possible obtain PSA samples before

anticoagulant therapy, may require samples. Some samples, particularly ensure that complete clot formation has presence of fibrin. To prevent erroneous complete clot forms may result in the Centrituging serum samples before a increased clotting time. those from patients receiving results due to the presence of fibrin, taken place prior to centrifugation of

than the total volume required.) cup must contain at least 100 μL more Volume Required: 10 µL serum. (Sample

assayed after extended storage. or at ~20°C or colder if samples are to be Storage: Stable at 2-8°C for 24 hours21

Warnings and Precautions

For in vitro diagnostic use.

accordance with applicable laws. Reagents: Store at 2-8°C. Dispose of in

tested and found nonreactive for syphilis; for antibodies to HIV 1 and 2; for hepatitis B surface antigen; and for antibodies to materials derived from human blood were transmitting infectious agents. Source all components as if capable of Follow universal precautions, and handle nepatitis C.

0.1 g/dL, has been added as a preservative. On disposal, flush with large Sodium azide, at concentrations less than volumes of water to prevent the buildup of

> and copper plumbing. potentially explosive metal azides in lead

contamination and exposure to direct sunlight. (See insert.) Chemiluminescent Substrate: Avoid

Water: Use distilled or deionized water.

Materials Supplied

barcode labels are needed for the assay. Components are a matched set. The

PSA antibody. Stable at 2-8°C until bead coated with with polyclonal goat anti-Each barcode-labeled unit contains one PSA Test Units (LPS1) LKPS1: 100 units. LKPS5: 500 units. expiration date.

ziplock ridge intact. Reseal the bags to cutting along the top edge, leaving the Allow the Test Unit bags to come to room protect from moisture. temperature before opening. Open by

after opening when stored as indicated. LKPS1: 1 wedge. LKPS5: 5 wedges. Recommended usage is within 30 days conjugated to monocional murine anti-Phosphatase (bovine calf intestine) PSA Reegent Wedge (LPS2) 2-8°C until expiration date. Store capped and refrigerated: Stable at With beroode, 6.5 mL alkaline PSA antibody in buffer, with preservative

Two vials (Low and High) 1.5 mL each of PSA in a chicken serum/buffer matrix, with at -20°C after opening, or for 6 months (aliquotted) preservative. Stable at 2-8°C for 30 days PSA Adjustors (LPSL, LPSH)

LKPS1: 1 set. LKPS5: 2 sets.

Supplied Separately Kit Components

or longer (aliquotted) at -20°C. Stable at 2-8°C for 30 days after opening serum/buffer matrix, with preservative. One vial 25 mL of a PSA-free chicken For the manual dilution of patient samples. PSA Sample Diluent (LPSZ)

LKPM: Probe Cleaning Kit LPWS2: Probe Wash Module LSUBX: Chemiluminescent Substrate

LCHx-y: Sample Cup Holders (barcoded)

LSCP: Sample Cups (disposable)
LSCC: Sample Cup Caps (optional) TMCO: Tri-level, human serum based

Also Required

multi-constituent control

Sample transfer pipets, distilled or deionized water, controls.

Assay Procedure

preparation, setup, dilutions, adjustment assay, and quality control procedures. See the IMMULITE Operator's Manual for:

Adjustment Interval: 4 weeks.

or sample pools with at least two levels Quality Control Samples: Use controls (low and high) of PSA

of Prostate Cancer **Expected Values in Detection**

3810 men, aged 50 or older. Of these, 64 (2%) were Asian; 242 (6%) were African prospective study performed at three patients also underwent digital rectal examination (DRE). Of these, 252 were American; 3483 (91%) were Caucasian; 7 purposes, samples were collected from clinical sites for prostate cancer detection In two retrospective studies and one no ethnic information. 3438 out of 3810 (<1%) were other and 14 (<1%) provided and/or suspicious DRE. The following biopsied for elevated (> 4.0 ng/mL) PSA table summarizes these clinical studies

2 0	9
Siope es	2
Prostas Cancers	2
% Positive Bu (95% C	

(2.3% - 51.8%)		0.4%	85.2%
18.2%	N	=	2928
		DRE -	PSA <= 4.0 DRE -
(22.5% - 35.5%)		54.1%	10.3%
28.8%	55	191	353
		DRE -	PSA > 4.0 DRE -
% Positive Biopsies (95% CI)	No. of Prostate Cancers	3 6 8 2 8 8	Subjects (%)

than DRE alone. PSA determinations detected 68% (55/81) of cancers that DRE more effective in detecting prostate cancer when used in conjunction with DRE, was detected 6% (5/81) of cancers that PSA suspicious DRE and a normal PSA may converse is also true: a subject with even if the DRE is negative. However, the 4 ng/mL may warrant additional testing did not; PSA elevations greater than The study demonstrated that PSA testing also require additional testing since DRE determinations did not

distribution of PSA values by age decade were identified as asymptomatic subjects In the same studies, 2928 participants biopsied as well as for those subjects who PSA and DRE, and therefore, were not clinical study who had both a negative of age-specific reference ranges are safe represent a truly normal population. There questionable whether these subjects interpreted with caution since it is indeed tree of prostate disease. no certainty that all of these subjects were were negative for cancer biopsy. There is for these asymptomatic subjects in the The following table contains the are presently no data proving that the use Therefore, these data should be

270 age group	60-69 age group	50-59 age group	All subjects	Distribution of PSA Levels
10	=======================================	1338	2928	>
1.40	1.20	0.93	1.00	PSA Medien
3.60	3.40	3.00	3.30	95" %He

patients were tested. Shown below is the 2618 samples collected from 1965 In studies performed at four clinical sites,

> this study. distribution of IMMULITE PSA results from

umber of ubjects /	9	† 5	6 1 2 1	10-20 20-40	ğ
emale Subjects	ect.	l	ects		
253/253	5 0%	9%	ş	ş	?
Healthy					
149/149	00%	8	3	3	3
Nonmalignant Diseases	ant Disc	2305			

78/76	Malignan	28/28	Nonmalic	149/149
100% 0%	Malignant Diseases	100% 0%	Nonmalignant Diseases	100% 0%
3	.	Ş	898	8
3		0%		ş
2		2		Ş
3		ş		3

	473/473	Healthy Male Subjects
	3 99.4% 0.6% 0	le Subje
	0.6%	Ç
	ş	
	Ş	
ĺ	3	- 1

548/548	Susm-uon
76.2% 19.3% 3.5%	Non-Malignant Diseases
3.5%	
0.9%	
Ş	

Other Prost	333/333	BY I
Other Prostatic Diseases	67.9% 25.8% 5.4% 0.9%	
	5.4%	
	0.9%	
	Ş	

Other Non	66/66
Ionprostatic Diseases	80.3% 18.2%
5	1.5% 0%
	3

105/758	Prostate C	274/274
105/758 54.8% 11.7% 10.7% 7.5% 15.3%	Prostate Cancer (serially monitored)	274/274 42.3% 21.2% 13.1% 7.3% 16.1%
10.7% 7.59	nonitored)	3.1% 7.39
× 15.3%		6 16.1%

17/174	Stage A	105/758
64.9% 9.8% 9.2% 3.5% 12.6%		8 54.8% 11.7% 10.7% 7.5% 15.3%
9.8%		Ξ,
9.2%	1	5 %
3.5%		7.5%
12.6%		15.3%

Stage B

54.0% 14%

1965/2618 1962 275	Total:	38/282	Stage D	19/102	Stage C	37/200 54.0% 14% 12% 8.5% 11.5%
1962		48.2%		56.9%		54.0%
275		48.2% 13.1% 11.7% 8.9% 18.0%		58.9% 6.9% 7.8% 8.8% 19.8%		14%
138		11.7%		7.8%		12%
23	1	8.9% %		3 3 3		8.5%
g				19.6%		11.5%

Consider these limits as guidelines only. Each laboratory should establish its own reterence ranges.

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Limitations

alone as a screening test for malignant disease. disease, nor should serum PSA be used presence or absence of malignant interpreted as absolute evidence for the Serum PSA concentrations should not be

complete clinical evaluation of the patient which may also include serial serum PSA massage, since manipulation of the biopsy, prostatectomy or prostatic Samples should be obtained before determinations.

recurrence should be based on a Prediction of malignant prostatic disease

prostate gland may lead to elevated PSA levels persisting up to 3 weeks. 18 PSA expression may be altered due to adequately reflect the presence of residual or recurrent disease. 23 includes hormonal therapy may not a prostatic cancer treatment which Consequently, a low PSA result following normonal therapy for prostate cancer.

may show erroneous results in such assays. 22.24 Therefore, results should be antibodies derived from mice. In particular, interference in immunoassays that employ mouse protein which can cause Some individuals have antibodies to antibodies (HAMA). These specimens specimens from patients who have therapy may contain human anti-mouse monodonal antibodies for diagnosis or received preparations of mouse interpreted with caution for such patients

can react with the immunoglobulins Heterophilic antibodies in human serum combination with the clinical examination purposes, the results obtained from this components can occur. For diagnostic been formulated to minimize the risk of anomalous result. These reagents have products can demonstrate this type of exposed to animals or animal serum 33.] Samples from patients routinely antibodies: a problem for all [See Boscato LM, Stuart MC. Heterophilic included in the assay components causing assay should always be used in interactions between rare sera and test interference potentially causing an immunoassays. Clin Chem 1988:34:27. interference with in vitro immunoassays. patient medical history, and other findings interference; however, potential

IMMULITE PSA

See Tables and Graphs for data gel barriers or clot-promoting additives.) otherwise noted, all were generated on serum samples collected in tubes without Results are expressed in ng/mL. (Unless representative of the assay's performance

0.04 - 150 ng/mL Working "Reportable" Range:

High-dose Hook Effect: Analytical Sensitivity: 0.03 ng/mL

of 3 lots at each of four sites, using 10 replicates per run. The within-run means and CVs were averaged across these 240 representing a broad spectrum of PSA values were assayed in 20 runs for each Intraessay (Within-Run): Samples runs. Results are expressed in ng/mL. None up to 20,000 ng/mL

ø	00	7	o	S	•	ω	N		
157	112	*		4.7	2.8	7	0.46	0.21	Mean
5.97	4.14	1.55	0.27	0.15	0.09	0.057	0.0207	0.0128	SO
3.8%	3.7%	3.5%	3.1%	3.2%	3.2%	<u>+.1</u> ×	4.5%	8.1 %	ç

set was reanalyzed to determine run-to-run CVs for samples assayed in singilizate. The results were averaged across the four interassey (Run-to-Run): The same data study sites and three lots. Results are expressed in ng/ml.

۵	œ	7	o	U	•	W	N	-	
157	112	1	CB	4.7	2.8	1.4	0.46	0.21	Mean
10.3	6.3	2.73	0.41	0.24	0.143	0.087	0.0304	0.0195	So
6.6%	5.6%	8.2%	1.7%	5.1%	5.1%	6.2%	6.6%	9.3%	S

Linearity: Samples were assayed under various dilutions. Results are expressed in ZØ/mL

			ω				N					0
1 in 8	2 5 8	5 8	ор Э.	- 5 8	20	\$ 5 4	œ 5	5 8	2 5 8	2.	هر 2.	Dilution
18. 4	40.5	76.3	15 0	11.0	21.7	45.5	81.2	12.5	23.2	47.3	81.1	Observed
 6.05	37.5	75.0	1	10.2	20.3	40.6	ł	10.1	20.3	40.5	1	Expected
98%	108%	102%	ı	108%	107%	112%	1	124%	114%	117%	1	%0/E

Recovery: Samples spiked 1 to 19 with three PSA solutions (50, 151 and 659 ng/ml.) were assayed.

			ω				N					
ဂ	œ	>	ı	ဂ	æ	>	ı	ဂ	œ	>	ı	Solution
6 0.3	33.6	29.4	27.7	51.1	30.2	27.1	26.2	32.6	6.8	2.6	0.32	Observed
59.3	33.9	28.8	ł	57.9	33.5	27.4	ı	33.3	7.9	2.8	ł	Expected
102%	99%	102%	i	88%	90%	99%	1	98%	86%	93%	1	% O/E

Specificity: The assay is highly specific for prostate-specific antigen.

NO: pot delantaria	Vincristine	Prolactin	PAP	Mitomycin C	Megesterol	Leuprolide acetate	Lactalbumin	нсе	Flutamide	5-Fluorouracii	Finasteride	Ferritin	Daxorubicin Hydrochloride	Doxazosin mesylate	Diethylstilbestrol	Cyclophosphamide	Cisplatin	CEA	Amethopterin	AFP	Compound
	1000000	56	8	100000	1000000	100000	1000000	10000	100000	1000000	10000000	10000	100000	1000000	10000000	1000000	100000	8	100000	10000	Added Added
	8	N O	Š	8	8	8	<u>v</u>	8	š	Š	Š	8	중	N O	8	N _O	N N	8	Š	NO	Percent Cross- reactivity

ND: not detectable

Hemolysis: No significant effect. Billrubin: No significant effect.

IMMIII TE DEA

using Deming regression analysis.
Samples used were within the working range of the assays. The table below nonisotopic PSA assays were compared Method Comparison: All four of DPC's

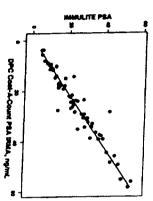
> regressions, with columns as Y, and rows presents the results of the Deming

Results of Deming Regressions

3rc		ITE 200 ration		3rd	IMM Gene	ULITE ration		. IM	MULI	TE 2	000	PSA	.	MMU	LITE	PSA		
Coefficient	(95% C)	(95% CI)	· 5	Coefficient	(95% CJ)	(95% CI)	3 3	Coefficient	(95% CI)	Intercept	(95% C))	3	Coefficient	(95% C)	(95% CI)	Slope	3	
0.991	-0.06 (-0.10 to -0.02)	0.92 (0.91 to 0.94)	473	0.993	-0.06 -0.02)	(1.00 to 1.03)	474	0.992	(0.06 to 0.16)	0.12	1.06	477					PSA	
0.990	-0.16 (-0.20 to -0.12)	0.86 (0.85 to 0.87)	473	0.988	-0.15 (-0.19 to -0.10)	0.94 (0.93 to 0.96)	474						0.992	(-0.15 to -0.07)	(0.93 to 0.95)	2 *	IMMULITE 2000 PSA	
0.990	0.00 (-0.04 to 0.04)	0.91 (0.90 to 0.92)	472					0.988	0.15 (0.11 to 0.20)	(1.05 to 1.08)	1.06	474	0.993 .	0.05 (0.02 to 0.09)	0.99 (0.98 to 1.00)	474	3rd Generation PSA	1M1: 77
				0.990	(-0.05 to 0.05)	1.10	472	0.990	0.18 (0.14 to 0.23)	(1.14 to 1.17)	1.16	3	0.991	0.06 (0.02 to 0.11)	1.08 (1.07 to 1.10)	473	3rd Generation PSA	

samples. (Concentration range: Coat-A-Count PSA IRMA on 69 patient The assay was also compared to DPC's approximately 5 to 55 ng/mL) By linear

(IML) - 0.92 (CAC IRMA) + 0.35 ng/mL



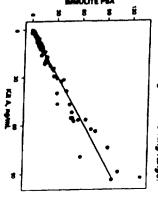
on different sets of patient serum samples studies were performed at different sites commercial kits, Kit A, Kit B and Kit C. The IMMULITE PSA was compared to three in three additional studies, DPC's dilution by that assay. Results were of the data encompassing different for purposes of the analysis. In each of subjected to linear regression analysis, (see Expected Values). Samples with PSA coefficient (r), and number of samples are or less. Slope, intercept, correlation involving an IMMULITE result of 20 ng/mL either assay, and (c) results for data pairs results not exceeding the working range of concentration ranges: (a) all results, (b) analysis was performed on three subsets these pairwise comparisons, regression assay being assigned that concentration with those below the detection limit of an range of an assay were reassayed under concentrations exceeding the working analyses, where tabulated below for each of these

Results are also displayed graphically for subsets (b) and (c). (See "Site 1", "Site 2" and "Site 3" graphs.) with the intercept expressed in ng/mL. IMMULITE = slope × (Kit X) + intercept

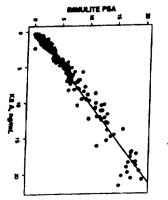
Site 1: Kit A

	T		Regu		_ ≥	L	
0.97	Results 52	1.06	ts Not Exce	1.01	leauts (PS,	Slope	
0.14	Results ≤20 ng/mL (by IMMUL/TE)	6.10	suits Not Exceeding Either Working Range	0.21	All Results (PSA Range: ND by IMM/JULITE	Intercept	
0.985	MAC	0.981	Workin	0.994	·	-	
%	ΠE)	673	g Range	710	-9567 ng/mL	5	
						_	

Site 1: IMMULITE PSA vs. Kit A Results not exceeding either working range:



Results <20 ng/mL (by IMMULITE):



regression:

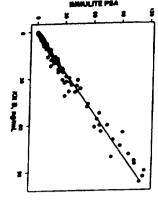
10.96

23.5 ng/mL (IMMULITE) 25.1 ng/mL (CAC IRMA

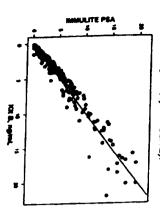
Site 3:

	2		Peaults 7	L	All Please	L
0.98	S S	1.16	Is Not Exce	=	P P	STOP
0.16	Results 520 ng/mil (by IMMULITE)	-0.27	eding Eith	J. 16	All Results (PSA Range: NO by MM/ULITE)	Intercept
0.981	וששטנו	0.992	Either Working Rung	0.998	10 - 6725 ng/mL E)	•
573	Ē	82	Range	2	3 €/mL	3

Results Not Exceeding Either Working Range. Site 2: MAMULITE PSA vs. Kit B

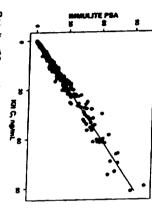


Results <20 ng/ml (by IMMULITE)

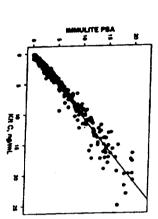


0.95	Result	0.99	Results Not Exceeding Either Working Range	0.96	All Results (PSA Range: ND by IMMULITE)	Slope
5	ğ	L	ğ	L	\$ E	*
0.07	Results 520 ng/mL (by IMMULITE)	0.01	eding Either	0.14	SA Range: ND by IMMULITE)	Intercept
0.987	MMULITE	0.993	Working	0.988) – 1061 ng/mL	1
1152		1239	Range	1261	DE/DE	3

Results Not Exceeding Either Working Range She 3: IMMULITE PSA vs. Kit C



Results <20 ng/mL (by IMMULITE)



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